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=> file caplus; d que l7; d que l10; d que l13
FILE 'CAPLUS' ENTERED AT 11:08:25 ON 16 APR 2003
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FILE COVERS 1907 - 16 Apr 2003  VOL 138 ISS 16
FILE LAST UPDATED: 15 Apr 2003  (20030415/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


L3          588 SEA FILE=CAPLUS ABB=ON  PLU=ON  BOTULINUM TOXIN (2A) A
L4       623803 SEA FILE=CAPLUS ABB=ON  PLU=ON  INJECT?
L5         8972 SEA FILE=CAPLUS ABB=ON  PLU=ON  PAIN/CT
L6        54461 SEA FILE=CAPLUS ABB=ON  PLU=ON  SPINE OR SPINAL
L7            3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 AND L4 AND L5 AND L6


L3          588 SEA FILE=CAPLUS ABB=ON  PLU=ON  BOTULINUM TOXIN (2A) A
L8         7718 SEA FILE=CAPLUS ABB=ON  PLU=ON  LUMBAR
L10           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 AND L8 AND PHARMAC?/SC,SX


L3          588 SEA FILE=CAPLUS ABB=ON  PLU=ON  BOTULINUM TOXIN (2A) A
L4       623803 SEA FILE=CAPLUS ABB=ON  PLU=ON  INJECT?
L6        54461 SEA FILE=CAPLUS ABB=ON  PLU=ON  SPINE OR SPINAL
L13           7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 AND L6 AND L4 AND PHARMAC?/S
                C,SX


=> s l7 or l10 or l13
L67           8 L7 OR L10 OR L13

=> file medline
FILE 'MEDLINE' ENTERED AT 11:08:49 ON 16 APR 2003

 FILE LAST UPDATED: 10 APR 2003 (20030410/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
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substance identification.

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=> d que l25; d que l26; d que l29
L14        1087 SEA FILE=MEDLINE ABB=ON  PLU=ON  BOTULINUM TOXIN TYPE A/CT
L15       56057 SEA FILE=MEDLINE ABB=ON  PLU=ON  SPINE+NT/CT
L16       53113 SEA FILE=MEDLINE ABB=ON  PLU=ON  SPINAL CORD+NT/CT
L17      116989 SEA FILE=MEDLINE ABB=ON  PLU=ON  MUSCLES/CT OR MUSCLES,
                SKELETAL+NT/CT
L18      165620 SEA FILE=MEDLINE ABB=ON  PLU=ON  INJECTIONS+NT/CT
L25           1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L14 AND (L15 OR L16 OR L17)
                AND L18

L14        1087 SEA FILE=MEDLINE ABB=ON  PLU=ON  BOTULINUM TOXIN TYPE A/CT
L15       56057 SEA FILE=MEDLINE ABB=ON  PLU=ON  SPINE+NT/CT
L16       53113 SEA FILE=MEDLINE ABB=ON  PLU=ON  SPINAL CORD+NT/CT
L17      116989 SEA FILE=MEDLINE ABB=ON  PLU=ON  MUSCLES/CT OR MUSCLES,
                SKELETAL+NT/CT
L19      156061 SEA FILE=MEDLINE ABB=ON  PLU=ON  PAIN+NT/CT
L26           1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L14 AND (L15 OR L16 OR L17)
                AND L19

L14        1087 SEA FILE=MEDLINE ABB=ON  PLU=ON  BOTULINUM TOXIN TYPE A/CT
L18      165620 SEA FILE=MEDLINE ABB=ON  PLU=ON  INJECTIONS+NT/CT
L19      156061 SEA FILE=MEDLINE ABB=ON  PLU=ON  PAIN+NT/CT
L28          27 SEA FILE=MEDLINE ABB=ON  PLU=ON  L14 AND L18 AND L19
L29           3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L28 AND (WHIPLASH OR NECK)/TI

=> s l25 or l26 or l29
L68           5 L25 OR L26 OR L29

=> file embase; d que l41
FILE 'EMBASE' ENTERED AT 11:09:37 ON 16 APR 2003
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 FILE COVERS 1974 TO 10 Apr 2003 (20030410/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L30        2380 SEA FILE=EMBASE ABB=ON  PLU=ON  BOTULINUM TOXIN A/CT
L31       35288 SEA FILE=EMBASE ABB=ON  PLU=ON  SPINE+NT/CT
L32       31399 SEA FILE=EMBASE ABB=ON  PLU=ON  SPINAL CORD+NT/CT
L33      239096 SEA FILE=EMBASE ABB=ON  PLU=ON  MUSCLE+NT/CT
L34       13133 SEA FILE=EMBASE ABB=ON  PLU=ON  INJECTION+NT/CT
L35      205153 SEA FILE=EMBASE ABB=ON  PLU=ON  PAIN+NT/CT
L41           5 SEA FILE=EMBASE ABB=ON  PLU=ON  L30 AND (L31 OR L32 OR L33)
                AND L34 AND L35 AND NECK MUSCLE/CT

=> file biosis; d que l54; d que l57
FILE 'BIOSIS' ENTERED AT 11:09:49 ON 16 APR 2003
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 9 April 2003 (20030409/ED)


L42         1034 SEA FILE=BIOSIS ABB=ON  PLU=ON  BOTULINUM TOXIN (2A) A
L43       145147 SEA FILE=BIOSIS ABB=ON  PLU=ON  SPINE OR SPINAL
L44        30737 SEA FILE=BIOSIS ABB=ON  PLU=ON  LUMBAR
L47       331046 SEA FILE=BIOSIS ABB=ON  PLU=ON  INJECT?
L48       126929 SEA FILE=BIOSIS ABB=ON  PLU=ON  PAIN
L54            4 SEA FILE=BIOSIS ABB=ON  PLU=ON  L42 AND (L43 OR L44) AND L47
                 AND L48



L42         1034 SEA FILE=BIOSIS ABB=ON  PLU=ON  BOTULINUM TOXIN (2A) A
L43       145147 SEA FILE=BIOSIS ABB=ON  PLU=ON  SPINE OR SPINAL
L44        30737 SEA FILE=BIOSIS ABB=ON  PLU=ON  LUMBAR
L48       126929 SEA FILE=BIOSIS ABB=ON  PLU=ON  PAIN
L55            8 SEA FILE=BIOSIS ABB=ON  PLU=ON  L42 AND (L43 OR L44) AND L48
L57            2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L55 AND BACK/TI


=> s l54 or l57
L69            5 L54 OR L57

=> file wpid; d que l66
FILE 'WPIDS' ENTERED AT 11:10:07 ON 16 APR 2003
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FILE LAST UPDATED:          10 APR 2003      <20030410/UP>
MOST RECENT DERWENT UPDATE:     200324        <200324/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L60           48 SEA FILE=WPIDS ABB=ON  PLU=ON  BOTULIN? TOXIN (2A) A
L61       392294 SEA FILE=WPIDS ABB=ON  PLU=ON  SPINE OR SPINAL OR BACK OR
                 LUMBAR
L62       280271 SEA FILE=WPIDS ABB=ON  PLU=ON  INJECT?
L65            7 SEA FILE=WPIDS ABB=ON  PLU=ON  L60 AND L61 AND L62
L66            5 SEA FILE=WPIDS ABB=ON  PLU=ON  L65 NOT (MUCUS OR HYPERHI?)/TI
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=> dup rem l68 l67 l41 l69 l66
FILE 'MEDLINE' ENTERED AT 11:10:35 ON 16 APR 2003

FILE 'CAPLUS' ENTERED AT 11:10:35 ON 16 APR 2003
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PROCESSING COMPLETED FOR L68
PROCESSING COMPLETED FOR L67
PROCESSING COMPLETED FOR L41
PROCESSING COMPLETED FOR L69
PROCESSING COMPLETED FOR L66
L70          25 DUP REM L68 L67 L41 L69 L66 (3 DUPLICATES REMOVED)
                ANSWERS '1-5' FROM FILE MEDLINE
                ANSWERS '6-13' FROM FILE CAPLUS
                ANSWERS '14-18' FROM FILE EMBASE
                ANSWERS '19-21' FROM FILE BIOSIS
                ANSWERS '22-25' FROM FILE WPIDS

=> d ibib ab l70 1-25

L70  ANSWER 1 OF 25     MEDLINE
ACCESSION NUMBER:    2002408778     MEDLINE
DOCUMENT NUMBER:     22152850   PubMed ID: 12162778
TITLE:               Head and neck muscle spasm after radiotherapy:
                     management with botulinum toxin A injection.
AUTHOR:              Van Daele Douglas J; Finnegan Eileen M; Rodnitzky Robert L;
                     Zhen Weining; McCulloch Timothy M; Hoffman Henry T
CORPORATE SOURCE:    Department of Otolaryngology-Head and Neck Surgery,
                     University of Iowa Health Care, Iowa City 52242, USA..
                     douglas-van-daele@uiowa.edu
SOURCE:              ARCHIVES OF OTOLARYNGOLOGY -- HEAD AND NECK SURGERY, (2002
                     Aug) 128 (8) 956-9.
                     Journal code: 8603209. ISSN: 0886-4470.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       (CLINICAL TRIAL)
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         200208
ENTRY DATE:          Entered STN: 20020807
                     Last Updated on STN: 20020829
                     Entered Medline: 20020827
AB   OBJECTIVE: To introduce the concept of neck muscle pain and spasm after
     radiotherapy and its treatment with botulinum toxin A.  DESIGN: Case
     series.  SETTING: Ambulatory patients at a tertiary care medical center.
     PATIENTS: Individuals who had undergone primary or adjuvant radiotherapy
     for treatment of carcinoma of the head and neck were asked about painful
     spasms of the neck musculature.  A volunteer sample was used.  If they
     desired treatment with botulinum toxin A, they were included in the study.
     INTERVENTION: Patients received botulinum toxin A injections to the
     affected sternocleidomastoid muscle(s) in 1 or 2 locations.  OUTCOME
```

MEASURE: Subjective pain relief. RESULTS: Four of 6 patients with painful tightness of the neck who received botulinum toxin A injections to the sternocleidomastoid muscle achieved pain relief. CONCLUSIONS: A subset of patients with irradiation-induced cervical muscle spasm benefit from treatment with botulinum toxin A injections. Further study is needed to more clearly define the entity and treatment.

L70 ANSWER 2 OF 25 MEDLINE
ACCESSION NUMBER: 2003059619 MEDLINE
DOCUMENT NUMBER: 22457384 PubMed ID: 12569964
TITLE: Use of botulinum toxin in chronic **whiplash** -associated disorder.
AUTHOR: Freund Brian J; Schwartz Marvin
CORPORATE SOURCE: The Crown Institute, Toronto, Ontario, Canada.. Freund@crowninstitute.com
SOURCE: CLINICAL JOURNAL OF PAIN, (2002 Nov-Dec) 18 (6 Suppl) S163-8.
Journal code: 8507389. ISSN: 0749-8047.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030207
Last Updated on STN: 20030319
Entered Medline: 20030318

AB Whiplash-associated disorders (WADs) occur as a result of trauma and are often due to motor vehicle accidents and sports injuries. Cervical injury is attributed to rapid extension followed by neck flexion. The exact pathophysiology of WAD is uncertain but probably involves some degree of aberrant muscle spasms and may produce a wide range of symptoms. Initial treatment of pain associated with whiplash usually includes oral medications, such as muscle relaxants and nonsteroidal anti-inflammatory drugs.. However, these agents are limited by potential systemic adverse effects. Some patients with chronic WAD may benefit from radiofrequency neurotomy. A new approach to treatment is the use of botulinum toxin, which acts to reduce muscle spasms. Type A toxin (Botox) has been studied in small trials of patients with WAD and has generally been found to relieve pain and improve range of motion. In addition, recent preliminary data from a small trial showed that type B toxin (Myobloc) produced almost immediate pain relief for most patients with post-whiplash headache. Although botulinum toxin has not been evaluated in large long-term trials, these initial data are promising and suggest a role for this agent in the treatment of WAD. Additional study is needed to identify the subset of patients with WAD who are most likely to respond to treatment with botulinum toxin.

L70 ANSWER 3 OF 25 MEDLINE
ACCESSION NUMBER: 1999188588 MEDLINE
DOCUMENT NUMBER: 99188588 PubMed ID: 10090202
TITLE: Treatment of **whiplash** associated **neck** pain with botulinum toxin-A: report of 8 cases.
AUTHOR: Freund B J; Schwartz M
SOURCE: JOURNAL OF RHEUMATOLOGY, (1999 Mar) 26 (3) 756-8.
Journal code: 7501984. ISSN: 0315-162X.
PUB. COUNTRY: Canada
DOCUMENT TYPE: (CLINICAL TRIAL)
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905

ENTRY DATE: Entered STN: 19990525
Last Updated on STN: 19990525
Entered Medline: 19990507

L70 ANSWER 4 OF 25 MEDLINE
ACCESSION NUMBER: 1998329455 MEDLINE
DOCUMENT NUMBER: 98329455 PubMed ID: 9664753
TITLE: Botulinum toxin A, adjunctive therapy for refractory headaches associated with pericranial muscle tension.
AUTHOR: Wheeler A H
CORPORATE SOURCE: Charlotte Spine Center, NC 28207, USA.
SOURCE: HEADACHE, (1998 Jun) 38 (6) 468-71.
Journal code: 2985091R. ISSN: 0017-8748.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980903
Last Updated on STN: 19980903
Entered Medline: 19980825

AB Pericranial muscle tension may contribute to the development of facial discomfort, chronic daily headache, and migraine-type headache. Elimination of pericranial muscle tension may reduce associated myalgia and counteract influences that can trigger secondary headaches which fall within the migraine continuum. Four patients with chronic, predominantly tension-type headaches and associated pericranial muscle tension failed prolonged conventional treatment and, therefore, symptomatic areas were treated with botulinum toxin A. This alleviated myalgia and reduced the severity and frequency of migraine-type headaches with a concomitant reduction in subsequent medical and physical therapy interventions. Judicious use of botulinum toxin A into defined areas of pericranial muscle tension may be useful for reducing primary myalgia and secondary headache.

L70 ANSWER 5 OF 25 MEDLINE
ACCESSION NUMBER: 97365352 MEDLINE
DOCUMENT NUMBER: 97365352 PubMed ID: 9222189
TITLE: Human response to botulinum toxin injection: type B compared with type A.
AUTHOR: Sloop R R; Cole B A; Escutin R O
CORPORATE SOURCE: Department of Neurology, Loma Linda University School of Medicine, CA 92354, USA.
SOURCE: NEUROLOGY, (1997 Jul) 49 (1) 189-94.
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970916
Last Updated on STN: 19970916
Entered Medline: 19970903

AB Despite the clinical potential of botulinum toxin type B (BTXB) for treating focal dystonia, hemifacial spasm, and other movement disorders, particularly in those resistant to botulinum toxin type A (BTXA), no objective human data exist to compare the muscle paralysis resulting from these two botulinum toxin subtypes. To objectively compare the human muscle paralysis resulting from intramuscular injections of BTXB with that

from BTXA, we measured the extensor digitorum brevis (EDB) M wave amplitude four times before and six times after injection with 17 different doses of BTXB (from 1.25 to 480 units) in 17 healthy volunteers. This established a dose-response curve that we compared with the previously published BTXA dose-response curve. After the establishment of the dose-response curve, we injected 10 new volunteers with five different doses of BTXB and BTXA measuring EDB M wave amplitude 4 times before and 13 times over 57 weeks after injection. The volunteers were randomized by dose and received BTXA and BTXB in opposite EDB muscles. The effect of the toxin in all volunteers was expressed as percent decline in M wave amplitude postinjection (% paralysis). The maximal paralysis 2 weeks postinjection with 320 to 480 mouse units (MU) of BTXB was 50 to 75%, whereas maximal paralysis was 70 to 80% with 7.5 to 10 MU of BTXA. Postexercise M wave facilitation on day 9 postinjection averaged 63% for BTXB and 20% for BTXA. Seven weeks postinjection, BTXB-induced paralysis had improved by 66% with complete improvement by 11 weeks postinjection, whereas BTXA-induced paralysis had improved by only 6% at 7 weeks, and at 57 weeks postinjection 22% of the original muscle paralysis was still present. Thus, human muscle paralysis resulting from BTXB injection is not as complete or long-lasting as that resulting from BTXA.

L70 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:434035 CAPLUS
DOCUMENT NUMBER: 135:267063
TITLE: **Botulinum toxin A** and chronic low back pain: A randomized, double-blind study
AUTHOR(S): Foster, Leslie; Clapp, Larry; Erickson, Marleigh; Jabbari, Bahman
CORPORATE SOURCE: Departments of Physical Medicine & Rehabilitation, Walter Army Medical Center, Washington, DC, USA
SOURCE: Neurology (2001), 56(10), 1290-1293
CODEN: NEURAI; ISSN: 0028-3878
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objectives: To investigate the efficacy of **botulinum toxin A** in chronic low back pain and assocd. disabilities. Methods: Thirty-one consecutive patients with chronic low back pain who met the inclusion criteria were studied: 15 received 200 units of **botulinum toxin** type **A**, 40 units/site at five **lumbar** paravertebral levels on the side of max. discomfort, and 16 received normal saline. Each patient's baseline level of pain and degree of disability was documented using the visual analog scale (VAS) and the Oswestry Low Back Pain Questionnaire (OLBPQ). The authors reevaluated the patients at 3 and 8 wk (visual analog scale) and at 8 wk (OLBPQ). Results: At 3 wk, 11 of 15 patients who received botulinum toxin (73.3%) had >50% pain relief vs. four of 16 (25%) in the saline group ($p = 0.012$). At 8 wk, nine of 15 (60%) in the botulinum toxin group and two of 16 (12.5%) in the saline group had relief ($p = 0.009$). Repeat OLBPQ at 8 wk showed improvement in 10 of 15 (66.7%) in the botulinum toxin group vs. three of 16 (18.8%) in the saline group ($p = 0.011$). No patient experienced side effects. Conclusion: Paravertebral administration of **botulinum toxin A** in patients with chronic low back pain relieved pain and improved function at 3 and 8 wk after treatment.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2001:864445 CAPLUS

DOCUMENT NUMBER: 137:119430
TITLE: **Botulinum toxin A** for the treatment of chronic neck pain
AUTHOR(S): Wheeler, Anthony H.; Goolkasian, Paula; Gretz, Stephanie S.
CORPORATE SOURCE: Charlotte Spine Center, Charlotte, NC, 28207, USA
SOURCE: Pain (2001), 94(3), 255-260
CODEN: PAINDB; ISSN: 0304-3959
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A clin. study tested the therapeutic efficacy of **Botulinum toxin A** (BTXA) when **injected** into symptomatic neck muscles after one **injection** session. Patients with chronic neck pain were randomly assigned to receive either a high dose of an active treatment or an **injection** of the same vol. of normal saline. Patients were compared for 4 mo using a comprehensive set of outcome measures that included the Neck Pain and Disability Scale (**Spine** 24 (1999) 1290) and pressure algometry (Arch Phys Med Rehabil 67 (1986) 406; Pain 30 (1987) 115; Clin J Pain 2 (1987) 207). Analyses were consistent in showing significant benefits from the **injection** session; however, the effects were not specific to the group treated with BTXA. Both treatment and control groups showed a significant decline in pain and disability across time and an increased ability to withstand pressure on trigger points. The heavy incidence of adverse events in the treatment group may partly explain the absence of a treatment effect specific to BTXA. The results show that a single dose treatment without phys. therapy is not effective for chronic neck pain.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 2000:622395 CAPLUS
DOCUMENT NUMBER: 133:187976
TITLE: Methods for treating pain with an intrathecally administered neurotoxin
INVENTOR(S): Aoki, Kei Roger; Cui, Minglei
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: U.S., 20 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6113915	A	20000905	US 1999-417195	19991012
WO 2001026736	A2	20010419	WO 2000-US12597	20000509
WO 2001026736	A3	20020321		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000049954	A5	20010423	AU 2000-49954	20000509
BR 2000014710	A	20020618	BR 2000-14710	20000509

EP 1237566 A2 20020911 EP 2000-932200 20000509
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
US 6235289 B1 20010522 US 2000-578097 20000525
US 6333037 B1 20011225 US 2000-578181 20000525
US 2001012828 A1 20010809 US 2001-797556 20010301
US 6372226 B2 20020416
PRIORITY APPLN. INFO.: US 1999-417195 A 19991012
WO 2000-US12597 W 20000509
US 2000-578097 A1 20000525

AB Methods are disclosed for treating pain by intrathecal administration to a human patient of a therapeutically effective amt. of a neurotoxin, e.g. **botulinum toxin** type **A**.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:222323 CAPLUS
DOCUMENT NUMBER: 138:231770
TITLE: Methods for treating fibromyalgia with Clostridial toxin
INVENTOR(S): Voet, Martin A.
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003054975	A1	20030320	US 2001-954610	20010917

PRIORITY APPLN. INFO.: US 2001-954610 20010917

AB Methods for treating fibromyalgia may include administering a therapeutically effective amt. of a Clostridial toxin to a peripheral location on the body of a patient. This peripheral location is other than the site on the body where the pain emanates. Patients were treated by i.m. or s.c. **injection** of **botulinum toxin** type **A** into regions near the tender points.

L70 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:241331 CAPLUS
DOCUMENT NUMBER: 136:273210
TITLE: Clostridial toxin derivatives and methods for treating pain
INVENTOR(S): Donovan, Stephen
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 625,098.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002037833	A1	20020328	US 2001-922093	20010803
US 6500436	B2	20021231		

PRIORITY APPLN. INFO.: US 2000-489667 A2 20000119

US 2000-625098 A2 20000725

AB Agents for treating pain, methods for producing the agents and methods for treating pain by administration to a patient of a therapeutically effective amt. of the agent are disclosed. The agent can include a clostridial neurotoxin, or a component or fragment or deriv. thereof, attached to a targeting moiety, wherein the targeting moiety is selected from a group consisting of transmission compds. which can be released from neurons upon the transmission of pain signals by the neurons, and compds. substantially similar to the transmission compds. The agent comprises **a botulinum toxin** component covalently coupled to substance P.

L70 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:605082 CAPLUS
DOCUMENT NUMBER: 137:163169
TITLE: Botulinum toxins in the treatment of cervical dystonia
AUTHOR(S): Hyman, Nigel
CORPORATE SOURCE: Dep. of Neurol., Radcliffe Infirmary, Oxford, UK
SOURCE: Round Table Series - Royal Society of Medicine Press (2002), 74(Optimal Patient Management with Botulinum Toxins: Evidence and Experience), 10-14
CODEN: RTMPFO; ISSN: 0268-3091
PUBLISHER: Royal Society of Medicine Press Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Botulinum toxin is the first treatment for cervical dystonia. Oral drugs are still used to treat the condition, but usually as an adjunct to.botulinum toxin in more resistant cases. The two com. available **botulinum toxin** type **A** products have different 'unit' potencies. Either 400 units of Dysport or 120 units of Botox would be used as an initial treatment for cervical dystonia. In our clinic, we started to use botulinum toxin type B (NeuroBloc) at 5000 units (1.0 mL) for treating this condition in type A resistant patients. However, at this dose the treatment was found not to be particularly effective, and hence the initial dose was increased to 10,000 units. Patients are usually re-booked for follow-up appointments at 12-14 wk. However, the duration of the effect of treatment varies between patients. He two most common muscles to **inject** are the sternocleidomastoid and splenius capitis, using a 0.5 x 16 needle. Side-effects are now uncommon due to an improved **injection** technique.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:834977 CAPLUS
DOCUMENT NUMBER: 135:71050
TITLE: **Botulinum toxin** type-**A** treatment in spastic paraparesis: a neurophysiological study
AUTHOR(S): Pauri, F.; Boffa, L.; Cassetta, E.; Pasqualetti, P.; Rossini, P. M.
CORPORATE SOURCE: Ospedale Fatebenefratelli, AFaR-CRCCS Centro di Ricovero e Cura a Carattere Scientifico: Divisione di Neurologia, Rome, 00186, Italy
SOURCE: Journal of the Neurological Sciences (2000), 181(1-2), 89-97
CODEN: JNSCAG; ISSN: 0022-510X
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: The aim of this study was to verify the action of

Botulinum toxin type-**A** (BoNT-A) by means of neurophysiol. techniques, in patients presenting lower limb spasticity and requiring BoNT-A **injections** in the calf muscles, due to the poor response to medical antispastic treatment. Subjects and method: Patients presenting paraparesis were enrolled. They underwent clin. evaluation for spasticity according to the Ashworth scale and neurophysiol. recordings including: motor evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) of the leg area; compd. motor action potential (cMAP) to tibial nerve stimulation, F-wave, and H-reflex before the treatment and 24 h, 2 wk and 1 mo after the **injection** of BoNT-A. In all patients, gastrocnemius was treated and in some cases soleus or tibialis posterior muscles were also **injected**. Results: In all patients, BoNT-A **injections** induced a clear clin. improvement as showed by the reduced spasticity values of the Ashworth scale. A significant increment of MEP latency and central conduction time (CCT) duration were obsd. 2 wk after the treatment only in the **injected** muscles. Conclusions: Prolonged MEP latencies and CCT after BoNT-A **injections** is probably due to a central alteration in responsiveness of **spinal** motor neurons to descending impulses from the corticospinal tracts. Such changes represent objective parameters heralding clin. efficacy of treatment.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:252612 CAPLUS
DOCUMENT NUMBER: 130:320763
TITLE: Botulinum toxin restores presynaptic inhibition of group la afferents in patients with essential tremor
AUTHOR(S): Modugno, Nicola; Priori, Alberto; Berardelli, Alfredo; Vacca, Laura; Mercuri, Bruno; Manfredi, Mario
CORPORATE SOURCE: Dipartimento di Scienze Neurologiche, Universita degli Studi di Roma "La Sapienza,", Rome, 00185, Italy
SOURCE: Muscle & Nerve (1998), 21(12), 1701-1705
CODEN: MUNEDE; ISSN: 0148-639X
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We studied the effect of **botulinum toxin A** **injection** on the abnormal presynaptic phase of reciprocal inhibition between forearm antagonist muscles in patients with essential tremor. Ten patients with essential tremor were investigated before and 1 mo after botulinum **injection**. Reciprocal inhibition was studied by conditioning the H reflex in forearm flexors with a radial-nerve stimulus delivered at a range of time intervals. **Botulinum toxin** produced **a** significant functional improvement in tremor (about 20%). Before botulinum toxin **injection**, patients had a reduced presynaptic phase of reciprocal inhibition. After botulinum toxin this phase was significantly more pronounced. The normal early disynaptic phase of reciprocal inhibition was normal before and after botulinum treatment. Although botulinum treatment reduced the size of the H reflex and the M wave to a similar extent, it left the H/M ratio unchanged. These findings show that botulinum toxin treatment restores presynaptic inhibition between forearm antagonist muscles. The results are also consistent with **botulinum toxin** having **a** beneficial effect in patients with essential tremor. Both effects probably depend upon the toxin's concurrent action on the extrafusal and intrafusal motor end-plates, the latter resulting in decreased spindle afferent input to the **spinal** cord.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 14 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003033371 EMBASE
TITLE: Discussion: Optimal doses for treatment with botulinum toxins.
AUTHOR: O'Brien C.
SOURCE: Round Table Series - Royal Society of Medicine, (2002) -/74 (64-76).
Refs: 1
ISSN: 0268-3091 CODEN: RTSSES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
011 Otorhinolaryngology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L70 ANSWER 15 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001440292 EMBASE
TITLE: Botulinum toxin type B: A new injectable treatment for cervical dystonia.
AUTHOR: Brashear A.
CORPORATE SOURCE: A. Brashear, Indiana Univ. School of Medicine, Department of Neurology, 550 University Boulevard, Indianapolis, IN 46202-5250, United States. abrashea@iupui.edu
SOURCE: Expert Opinion on Investigational Drugs, (2001) 10/12 (2191-2199).
Refs: 33
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cervical dystonia (CD) causes involuntary muscle spasms and is often associated with pain. Recently, botulinum toxin type B (BTX-B) (Myobloc.RTM., Elan South San Francisco, CA, USA) was approved for general use in the treatment of CD in the USA. In two large pivotal trials, BTX-B was found to be safe and effective in decreasing the movements, pain and disability associated with CD. Benefits were noted both in patients who no longer respond and in those who continue to respond to botulinum toxin type A (BTX-A). BTX-B offers an additional therapeutic option for patients with CD.

L70 ANSWER 16 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001424807 EMBASE
TITLE: Botulinum toxin for the treatment of cervical dystonia.
AUTHOR: Tintner R.; Jankovic J.
CORPORATE SOURCE: J. Jankovic, Parkinson's Dis. Ctr./Move. Dis Clin, Department of Neurology, Baylor College of Medicine, 6550 Fannin, Houston, TX 77030, United States. josephj@bcm.tmc.edu
SOURCE: Expert Opinion on Pharmacotherapy, (2001) 2/12 (1985-1994).
Refs: 83
ISSN: 1465-6566 CODEN: EOPHF7
COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cervical dystonia (CD) manifests clinically through involuntary spasms of neck muscles, producing abnormal head and neck movements and postures, which is often associated with pain. CD is the most common form of focal dystonia presenting to movement disorders clinics. Chemodenervation with botulinum toxin (BTX) has become the first-line treatment for CD, producing satisfactory relief of symptoms in > 80% of cases. Unresolved issues that may impact on the overall results include the method of selection for injection sites (clinical vs. electromyography), dosing, dilution and the role and relative efficacy of the different BTX serotypes. A guiding therapeutic principle of BTX injections is to achieve optimal results with the lowest possible dosage and frequency of administration. This strategy is critical in order to keep the risk of immunoresistance at a minimum. Development of antibodies that block the effects of BTX, usually associated with frequent injections of high doses, is the main reason for secondary unresponsiveness to this treatment. Although the mechanism of denervation at the neuromuscular junction by BTX is relatively well understood, the role of changes in muscle spindles and myopathic pain mechanisms, as well as secondary changes at the level of the basal ganglia, thalamus and cortex and their role in response to BTX, all need further exploration.

L70 ANSWER 17 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999228419 EMBASE
TITLE: [The use of botuline A toxin in the treatment of myofascial painful syndromes].
L'IMPIEGO DELLA TOSSINA BOTULINICA TIPO A NELLE SINDROMI DOLOROSE MIOFASCIALI.
AUTHOR: Porta M.; Loiero M.; Gamba M.; Luccarelli G.; Fornari M.
CORPORATE SOURCE: Prof. M. Porta, Centro del Dolore, Divisione Neurologica, Policlinico San Marco, c.so Europa 7, 24040 Zingonia BG, Italy
SOURCE: Riabilitazione, (1999) 32/2 (49-55).
Refs: 15
ISSN: 0557-9430 CODEN: RIBZAJ
COUNTRY: Italy
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
019 Rehabilitation and Physical Medicine
037 Drug Literature Index
052 Toxicology
LANGUAGE: Italian
SUMMARY LANGUAGE: English; Italian
AB Myofascial pain syndrome (MPS) is a common illness. The pathophysiology of MPS remains unclear. Previous preliminary studies have demonstrated therapeutic efficacy of the muscle relaxant botulinum toxin type A (BTX-A) in the treatment of MPS. A single-centre, randomised trial was undertaken to compare the effects of BTX-A with the steroid methylprednisolone (both administered with 50% bupivacaine), combined with post-injection physiotherapy, in 40 patients suffering from chronic myofascial pain in the piriformis, iliopsoas or scalenus anterior muscles. Thirty days after receiving an injection of either BTX-A or steroid, pain severity had decreased significantly from baseline in both treatment groups. However, the baseline pain score was significantly higher in the BTX-A treatment

group compared with the steroid group, and the reduction in pain score between baseline and 30 days post-injection was greater in the BTX-A group compared with the steroid group (p = 0.0598). At 60(th) days post-injection, the pain severity score for the BTX-A treated patients was statistically significantly lower than the pain score for the steroid-treated population. Furthermore. the reduction in pain score in the BTX-A group at 60(th) days post-injection was greater than at 30(th) days, whereas the effect of the steroid had begun to wane.

L70 ANSWER 18 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998085413 EMBASE
TITLE: Guidelines for the therapeutic use of botolinum toxin in movement disorders.
AUTHOR: Berardelli A.; Abbruzzese G.; Bertolasi L.; Cantarella G.; Carella F.; Curra A.; De Grandis D.; DeFazio G.; Galardi G.; Girlanda P.; Livrea P.; Modugno N.; Priori A.; Ruoppolo G.; Vacca L.; Manfredi M.
CORPORATE SOURCE: Dr. A. Berardelli, Dipartimento di Scienze Neurologiche, Universita di Roma 'La Sapienza', Viale dell'Universita 30, 00185 Roma, Italy
SOURCE: Italian Journal of Neurological Sciences, (1997) 18/5 (261-269).
Refs: 74
ISSN: 0392-0461 CODEN: IJNSD3
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
008 Neurology and Neurosurgery
019 Rehabilitation and Physical Medicine
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English; Italian
AB Since its introduction in the early '80s the use of botulinum toxin has improved the quality of life of the patients affected by movement disorders. Toxin's neuromuscular blocking action allows a symptomatic treatment of those clinical conditions characterised by excessive muscular activity. Although the dosages used are safe and the side-effects are reversible, a correct use of botulinum toxin depends on the knowledge of its clinical pharmacology and of the anatomy of the body segments to be injected. In addition, the treatment of more complex conditions, i.e. laringeal dystonia, imposes an inter-disciplinary approach and specialised injection techiques. In this review, the Italian Study Group on Movement Disorders presents the consensus guidelines for the therapeutic use of botulinum toxin in movement disorders. The main toxin types, their use and administration modalities, and the training guidelines will be presented.

L70 ANSWER 19 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2003:90015 BIOSIS
DOCUMENT NUMBER: PREV200300090015
TITLE: Treatment of Chronic Low **Back Pain** by Local **Injection** of **Botulinum Toxin A.**
AUTHOR(S): Subin, Bill (1); First, Georgia A. Morgan (1); Cork, Randall C. (1)
CORPORATE SOURCE: (1) Anesthesiology, LSU Health Sciences Center, Shreveport, LA, USA USA
SOURCE: Anesthesiology Abstracts of Scientific Papers Annual Meeting, (2002) No. 2000, pp. Abstract No. 771. http://www.asa-abstracts.com. cd-rom.
Meeting Info.: 2000 Annual Meeting of the American Society

of Anesthesiologists San Francisco, CA, USA October 16-18, 2000 American Society of Anesthesiologists Inc.

DOCUMENT TYPE: Conference
LANGUAGE: English
AB Introduction. Since the initial use of **Botulinum Toxin A** (BTA) in the treatment of strabismus 20 years ago, is has also been used to treat spasticity, cervical dystonia, spasmodic dystonia, writer's cramp, and tremor.1-3 However, use of BTA in the treatment of fibromyalgia, myofascial **pain** and chronic low back **pain** is still controversial. In order to clarify the effects of BTA on the low back **pain** secondary to myoneural syndrome and **lumbar** radiculitis, we studied its use in a group of chronic **pain** patients at LSU Health Sciences Center from 1998 to the present. Material and Methods. With IRB approval and following informed consent, nineteen patients diagnosed with myoneural syndrome and/or **lumbar** radiculitis were enrolled in this study and followed for 6-12 months. Data were collected using the following methods: Visual Analogue Scale (0-10), McGill-Melzack **Pain** Questionnaire, Oswestry Disability Questionnaire, Roland-Morris Disability Scale, and a muscle spasm score (0-4). Patients provided these data upon referral and then again either 1 month after treatment (BTA group) or within 1-12 months of referral (control group). An assessment of the range of the patient's range of motion was also done. Scales that use physical measures to quantify the effects of **pain** have certain criteria similar to those of self-reported scales. There were 10 patients in the control (non-treated) group. In the BTA group, 9 patients were treated with local **injections** of **Botulinum Toxin A** (BTX-**A**, Allergan Pharmaceuticals, Porton Products Pharmaceuticals, Ltd). Results. Comparison of the two sets of data for the control group demonstrated that, during the period between questionnaires, the natural progression of untreated chronic low back **pain** was generally to become worse. However, the patients treated with BTA showed an overall improvement (Table 1). Conclusions. Although the number of cases in this study is limited, it appears that the beneficial effect of BTA in the relaxation of muscle spasm associated with chronic low back **pain** leads to **pain** relief. Further investigation should be encouraged.

L70 ANSWER 20 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:158342 BIOSIS
DOCUMENT NUMBER: PREV200000158342
TITLE: Treatment of chronic cervical-associated headache with **botulinum toxin A: A** pilot study.
AUTHOR(S): Freund, Brian J. (1); Schwartz, Marvin
CORPORATE SOURCE: (1) 944 Merritton Road, Suite 100, Pickering, ON, L1V 1B1 Canada
SOURCE: Headache., (March, 2000) Vol. 40, No. 3, pp. 231-236. ISSN: 0017-8748.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: To see whether therapy with **botulinum toxin A** may prove to be an effective treatment for headache of musculoskeletal origin. Background: Headache is a common finding associated with neck injury. Cervicogenic headache, which is believed to be attributable to injury of the ligaments, muscles, or joints of the cervical **spine**, is centered in the occipital region with **pain** referred to the frontotemporal region. **Botulinum toxin A** produces prolonged muscle relaxation, which is

dose dependent and can be easily targeted to affected muscles. Methods: This randomized, double-blind, placebo-controlled study compares outcome measures in 26 patients suffering from chronic headache subsequent to a cervical whiplash injury. One half of the patients received **botulinum toxin A**, 100 units, diluted in 1 mL of saline, while the other half received just saline (1 mL). Five cervical trigger points received 0.2 mL each of **injectant** via a 30-gauge needle. Outcome measures included subjective head **pain** based on visual analog scales, as well as range of neck motion. Follow-up assessments were carried out at 2 and 4 weeks after treatment. Results: Fourteen subjects who received **botulinum toxin A** and 12 who received saline completed the study. At both 2 and 4 weeks post **injection**, the treatment group showed a significant improvement in **pain** and range of motion from preinjection levels ($P<.01$). The placebo group demonstrated no statistically significant changes at any posttreatment time.

L70 ANSWER 21 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:61868 BIOSIS
DOCUMENT NUMBER: PREV199900061868
TITLE: Has botulinum toxic type A a place in the treatment of spasticity in **spinal** cord injury patients.
AUTHOR(S): Al-Khodairy, A. T. (1); Gobelet, C.; Rossier, A. B.
CORPORATE SOURCE: (1) Chemin de Barrieres 35, CH-1920 Martigny Switzerland
SOURCE: Spinal Cord, (Dec., 1998) Vol. 36, No. 12, pp. 854-858. ISSN: 1362-4393.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Objective: To present and discuss treatment of severe spasms related to **spinal** cord injury with **botulinum toxin** type **A**. Design: A 2-year follow-up study of an incomplete T12 paraplegic patient, who was reluctant to undergo intrathecal baclofen therapy, presenting severe painful spasms in his lower limbs treated with intramuscular **injections** of **botulinum toxin** type **A**. Setting: Department of Physical Medicine and Rehabilitation, Hopital de Gravelone, Sion, Switzerland. Subject: Single patient case report. Main outcome measure: Spasticity, spasms and **pain** measured with the modified Ashworth scale, spasm frequency score and visual analogue scale. Results: Treatment of spasticity with selective intramuscular **injections** of **botulinum toxin** type **A** resulted in subjective and objective improvement. Conclusion: **Botulinum toxin** type **A** has its place in the treatment of spasticity in **spinal** cord injury patients. This treatment is expensive and its effect is reversible. It can complement intrathecal baclofen in treating upper limb spasticity in tetraplegic patients. Tolerance does occur to the toxin. Although high doses of the product are well tolerated, the quantity should be tailored to the patient's need. The minimal amount necessary to reach clinical effects should be adhered to and booster doses at short period intervals should be avoided.

L70 ANSWER 22 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2003-239131 [23] WPIDS
DOC. NO. CPI: C2003-061234
TITLE: Novel modified botulinum or tetanus toxin useful for treating disorders associated with inappropriate muscle contraction, comprises a botulinum or tetanus toxin coupled to polyethylene glycol.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): ALLISON, A
PATENT ASSIGNEE(S): (SURR-N) SURROMED INC

COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003000193	A2	20030103	(200323)*	EN	9
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW					
US 2002197278	A1	20021226	(200323)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003000193	A2	WO 2002-US19785	20020621
US 2002197278	A1 Provisional	US 2001-299807P	20010621
		US 2002-176957	20020621

PRIORITY APPLN. INFO: US 2001-299807P 20010621; US 2002-176957 20020621

AB WO2003000193 A UPAB: 20030407
NOVELTY - **A** modified **botulinum toxin** (I) comprising a botulinum toxin coupled to polyethylene glycol (PEG) or a modified tetanus toxin comprising a tetanus toxin coupled to PEG, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a pharmaceutical composition (II) comprising an effective amount of (I).

ACTIVITY - Analgesic; Laxative; Relaxant.

No biological data is given.

MECHANISM OF ACTION - None given.

USE - (I) or (II) is useful for treating a subject suspected of having a disorder of inappropriate muscle contraction, by administering a therapeutically effective amount of (I) to the patient. The disorder of inappropriate muscle contraction is selected from low **back** pain, cervical dystonia, constipation, cerebral palsy, spastic paresis, blepharospasm, strabismus, hyperhydrosis, hypersialorrhoea, whiplash, migration headache and tension headache. (I) is useful for treating a patient for a cosmetic purpose, by administering an effective amount of (I) to the patient, where the cosmetic purpose is the reduction of facial wrinkles. (All claimed.)

ADVANTAGE - The efficacy of (I) for the treatment of disorders associated with inappropriate muscle contraction and for cosmetic applications is improved, due to its modification. The side effects of (I) is decreased and its clinical utility is prolonged, due to its modification. Pegylation of (I) increases its molecular weight and decreases its diffusion from the **injection** site, thereby reducing side effects. The reduced immunogenicity of the pegylated toxin decreases the development of resistance.

Dwg.0/0

L70 ANSWER 23 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-502158 [55] WPIDS
CROSS REFERENCE: 2000-610759 [51]; 2002-178612 [08]
DOC. NO. CPI: C2001-150983
TITLE: Treatment of pain e.g. inflammatory pain involves intraspinal administration of a neurotoxin to a mammal.
DERWENT CLASS: B04

INVENTOR(S): AOKI, K R; CUI, M
PATENT ASSIGNEE(S): (AOKI-I) AOKI K R; (CUIM-I) CUI M; (ALLR) ALLERGAN SALES INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2001012828	A1	20010809	(200155)*		20
US 6372226	B2	20020416	(200232)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2001012828	A1	Cont of	US 1999-417195	19991012
		Cont of	US 2000-578097	20000525
			US 2001-797556	20010301
US 6372226	B2	Cont of	US 1999-417195	19991012
		Cont of	US 2000-578097	20000525
			US 2001-797556	20010301

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2001012828	A1	Cont of	US 6113915
		Cont of	US 6235289
US 6372226	B2	Cont of	US 6113915
		Cont of	US 6235289

PRIORITY APPLN. INFO: US 1999-417195 19991012; US 2000-578097 20000525; US 2001-797556 20010301

AB US2001012828 A UPAB: 20020521
NOVELTY - Treatment of pain or in vivo attenuation of a nociceptive activity or experience of a human patient involves the step of intraspinal administration of neurotoxin (preferably botulinum) to a mammal. Neurotoxin is free of any neuronal targeting group.

ACTIVITY - Analgesic; Antiinflammatory.

A patient, age 51, experiencing pain subsequent to injury to his hand, arm, foot or leg was treated by intrathecal administration e.g. by **spinal**, tap or by catheterization to the **spinal** cord, such as the **lumbar** region of the **spinal** cord, with **botulinum toxin** type **A** (0.1 - 30 U/kg). Within 1 - 7 days after toxin administration the patient's pain is subsequently alleviated.

MECHANISM OF ACTION - None given.

USE - In pharmaceutical preparation for the in vivo attenuation of a nociceptive activity (such as neuropathin pain syndrome and inflammatory pain) or experience of a human patient, for improving patient function and for treating pain (all claimed) such as pain subsequent to **spinal** cord injury or limb injury, pain associated with cancer and diabetes.

ADVANTAGE - There is improvement observed in at least one of factors of reduced pain, reduced time spent in bed, increased ambulation, healthier attitude and a more varied lifestyle, after intraspinal administration of neurotoxin. The administration of neurotoxin gives long duration of activity, low rates of diffusion out of an intrathecal space where administered, low rates of diffusion to other intrathecal areas outside of the site of administration. The method had limited or insignificant side effects at therapeutic dose levels. The method provides significant pain alleviation even though the neurotoxin is not

administrated in conjunction with any non-native or non-inherent to the neurotoxin neuronal targeting moiety. By intraspinal neurotoxin administration the symptoms of pain can be dramatically reduced for 2 - 4 months per **injection** of neurotoxin and pain alleviating effect persists for up to 10 days (preferably 20 days, especially 3 months). The **injected** neurotoxin tends to exert a CNS (central nervous system) site specific antinociceptive effect. The amount of neurotoxin **injected** intraspinally can be considerably less than the amount of the same neurotoxin required by other routes of administration i.e. intramuscular intrasphincter, oral or parenteral to achieve a comparable effect.
Dwg.0/7

L70 ANSWER 24 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-178612 [23] WPIDS
CROSS REFERENCE: 2000-610759 [51]; 2001-502158 [53]
DOC. NO. CPI: C2002-055267
TITLE: Treating pain with recombinant botulinum toxin, administered into the **spine** or to a dorsal root ganglion, has a long-lasting action without side effects.
DERWENT CLASS: B04 D16
INVENTOR(S): AOKI, K R; CUI, M
PATENT ASSIGNEE(S): (ALLR) ALLERGAN SALES INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6333037	B1	20011225	(200223)*		20

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6333037	B1	Div ex	US 1999-417195	19991012
			US 2000-578181	20000525

PRIORITY APPLN. INFO: US 1999-417195 19991012; US 2000-578181 20000525
AB US 6333037 B UPAB: 20020411
NOVELTY - Treatment of pain comprises administration of recombinantly produced botulinum toxin (rBT), not attached to a neuronal targeting component, either intraspinally or to a dorsal root ganglion.
ACTIVITY - Analgesic.
Inflammatory pain was induced in rats by subcutaneous **injection** of 5% formalin (50 micro l) into the paw. Intrathecal administration, near the **lumbar** enlargement, of Botox (RTM for **botulinum toxin** type **A**) at 0.625 unit (U)/kg 2-5 hr before **injection** of formalin reduced the time of the flinching/licking response to below 50 sec at all times over the 1 hr test period. For animals given saline only, the corresponding time was 250 sec initially and over 150 sec for most of the test period. Even when administered 14 days before **injection** of formalin, the toxin had a significant analgesic effect.
MECHANISM OF ACTION - Probably rBT specifically inhibits release of neurotransmitters from central terminal afferent sensory neurons and/or second-order projecting neurons in the dorsal horn.
USE - rBT is used to treat or prevent pain, especially neuropathic or inflammatory pain but also that associated with cancer, diabetes or other diseases.

A patient with acute inflammatory pain was treated by intrathecal administration (by **spinal** tap to the **lumbar** region) with 0.1-30 units/kg of **botulinum toxin** type **A** . Within 1-7 days substantial alleviation of pain was achieved.

ADVANTAGE - rBT has a long-lasting analgesic action, preferably up to 3 months. Even without a neuronal targeting component is diffuses only slowly from the site of **injection**; has only limited side effects, and doses required for intraspinal administration are lower than those for other routes of administration.

Dwg.0/7

L70 ANSWER 25 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-271251 [23] WPIDS
DOC. NO. CPI: C2000-082761
TITLE: Stable liquid pharmaceutical botulinum toxin formulation, useful for treating spasticity due to stroke, **spinal** cord injury, closed head trauma, cerebal palsy, multiple sclerosis, or Parkinson's disease.
DERWENT CLASS: B04
INVENTOR(S): HIRTZER, P; MOYER, E
PATENT ASSIGNEE(S): (ELAN-N) ELAN PHARM INC
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000015245	A2	20000323	(200023)*	EN	34
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9958214	A	20000403	(200034)		
NO 2001001207	A	20010509	(200134)		
BR 9913585	A	20010605	(200138)		
CZ 2001000564	A3	20010613	(200138)		
EP 1112082	A2	20010704	(200138)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
SK 2001000313	A3	20011008	(200163)		
CN 1316906	A	20011010	(200207)		
KR 2001086388	A	20010910	(200219)		
HU 2001003638	A2	20020128	(200222)		
EP 1112082	B1	20020731	(200257)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
DE 69902396	E	20020905	(200266)		
JP 2002524527	W	20020806	(200266)		46
AU 755556	B	20021212	(200305)		
ES 2181473	T3	20030216	(200321)		
ZA 2001001709	A	20030226	(200321)		51

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000015245	A2	WO 1999-US20912	19990909
AU 9958214	A	AU 1999-58214	19990909
NO 2001001207	A	WO 1999-US20912	19990909
		NO 2001-1207	20010309
BR 9913585	A	BR 1999-13585	19990909

		WO 1999-US20912	19990909
CZ 2001000564	A3	WO 1999-US20912	19990909
		CZ 2001-564	19990909
EP 1112082	A2	EP 1999-945649	19990909
		WO 1999-US20912	19990909
SK 2001000313	A3	WO 1999-US20912	19990909
		SK 2001-313	19990909
CN 1316906	A	CN 1999-810739	19990909
KR 2001086388	A	KR 2001-703032	20010309
HU 2001003638	A2	WO 1999-US20912	19990909
		HU 2001-3638	19990909
EP 1112082	B1	EP 1999-945649	19990909
		WO 1999-US20912	19990909
DE 69902396	E	DE 1999-602396	19990909
		EP 1999-945649	19990909
		WO 1999-US20912	19990909
JP 2002524527	W	WO 1999-US20912	19990909
		JP 2000-569829	19990909
AU 755556	B	AU 1999-58214	19990909
ES 2181473	T3	EP 1999-945649	19990909
ZA 2001001709	A	ZA 2001-1709	20010228

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9958214	A	Based on	WO 200015245
BR 9913585	A	Based on	WO 200015245
CZ 2001000564	A3	Based on	WO 200015245
EP 1112082	A2	Based on	WO 200015245
SK 2001000313	A3	Based on	WO 200015245
HU 2001003638	A2	Based on	WO 200015245
EP 1112082	B1	Based on	WO 200015245
DE 69902396	E	Based on	EP 1112082
		Based on	WO 200015245
JP 2002524527	W	Based on	WO 200015245
AU 755556	B	Previous Publ.	AU 9958214
		Based on	WO 200015245
ES 2181473	T3	Based on	EP 1112082

PRIORITY APPLN. INFO: US 1998-99870P 19980911

AB WO 200015245 A UPAB: 20000516

NOVELTY - A stable liquid pharmaceutical botulinum toxin formulation (I), comprising a buffer giving a pH range of 5 to 6 and isolated botulinum toxin, stable at a temperature of 0 to 30 deg. C for at least 1 year, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of treating a patient requiring inhibition of cholinergic input to a muscle, gland, or organ comprising administering (I).

ACTIVITY - Relaxant; cerebroprotective; neuroprotective; antiparkinsonian; analgesic; antimigraine; antiasthmatic.

Twenty-eight patients with a mean age of 50.9 with a confirmed diagnosis of cervical dystonia, received **injections** of botulinum toxin Type B formulation into 2-4 superficial neck and shoulder muscles with escalating doses (up to 1.5 fold per successive session) over time. Clinical benefit was assessed using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)-Severity test, with 25% reduction in score considered an improvement. Patients participated in the study from 28 to 177 days with a mean time in the study of 71.9 days. Patients were treated with 1 to 3 doses of formulation. Cumulative doses ranged from 1430 U to 12000 U, with individual doses ranging from 300 U to 12000 U.

For purposes of clinical assessment, 4 dose groups were defined: 100-800 U (Group A), 900-2399 U (Group B), 2400-5999 U (Group C), and 6000-12000 U (Group D). The length of time between dosing sessions ranged as follows: Group A, 13-101 days; Group B, 14-113 days; Group C, 29-177 days; and Group D, 28-177 days. Mean baseline scores were similar in all patients in all treatment groups, and all 4 groups experienced a mean decrease in score (improvement) during the study. Overall, mean percent improvement from baseline and mean response ratio for severity score was greatest in Groups C and D during the study. Measures of mean maximum improvement, mean maximum percent improvement and mean maximum response ratio were greater for the two higher dose groups (8.1 and 6.8 against 2.1 and 3.6 for maximum improvement). The percentage of patients responding to treatment was greater for the two higher dose groups (80 and 78% for C and D, respectively compared to 0 and 27% for A and B, respectively). The results therefore showed a dose-dependent response to botulinum B toxin formulations.

MECHANISM OF ACTION - (I) inhibits cholinergic input into muscles, glands and organs.

USE - The composition is useful for treating spasticity (due to stroke, **spinal** cord injury, closed head trauma, cerebal palsy, multiple sclerosis, or Parkinson's), blepharospasm, strabismus, hemifacial spasm, dystonia, otitis media, spastic colitis, anismus, urinary detrusor-sphincter dyssynergia, jaw-clenching, and curvature of the **spine**. (I) is also useful for treatment of myofascial pain, headache associated with migraine, vascular disturbances, neuralgia, neuropathy, arthrotos pain, **back** pain, hyperhydrosis, rhinnorhea, asthma, excessive salivation, and excessive stomach acid secretion.

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